Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1	("20030162231").PN.	US-PGPUB; USPAT; EPO	OR	OFF	2005/05/06 11:00
L2	2	((polyglutamine adj1 repeat) or (CAG adj1 repeat) or polyGln) same diameter	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/05/06 11:31
L3	55	((polyglutamine adj1 repeat) or (CAG adj1 repeat) or polyGln) and diameter	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/05/06 11:02
L4	3	l3 and filament	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2005/05/06 11:03
L5	38	((polyglutamine adj1 repeat) or (CAG adj1 repeat) or polyGln) and (TFA or (trifluoroacetic adj1 acid))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/06 11:48
L6	3	l5 and filament	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/06 11:38
L7	3	((polyglutamine adj1 repeat) or (CAG adj1 repeat) or polyGln) and (hexafluoroisopropanol or HFIP)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/06 11:48

FILE 'MEDICONF' ENTERED AT 11:52:32 ON 06 MAY 2005
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FILE 'PASCAL' ENTERED AT 11:52:32 ON 06 MAY 2005
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by means of any process and on any support whatsoever
is prohibited without the prior written agreement of INIST-CNRS.
COPYRIGHT (C) 2005 INIST-CNRS. All rights reserved.

=> ((polyglutamine adj1 repeat) or (CAG adj1 repeat) or polyGln) and (hexafluoroisopropanol or HFIP)
L7 0 FILE AGRICOLA
L8 0 FILE BIOTECHNO
L9 0 FILE CONFSCI
L10 0 FILE HEALSAFE
L11 0 FILE IMSDRUGCONF
L12 0 FILE LIFESCI
L13 0 FILE MEDICONF
L14 0 FILE PASCAL

TOTAL FOR ALL FILES
L15 0 ((POLYGLUTAMINE ADJ1 REPEAT) OR (CAG ADJ1 REPEAT) OR POLYGLN) AND (HEXAFLUOROISOPROPANOL OR HFIP)

=> ((polyglutamine repeat) or (CAG repeat) or polyGln) and (TFA or (trifluoroacetic acid))
L16 0 FILE AGRICOLA
L17 2 FILE BIOTECHNO
L18 0 FILE CONFSCI
L19 0 FILE HEALSAFE
L20 0 FILE IMSDRUGCONF
L21 0 FILE LIFESCI
L22 0 FILE MEDICONF
L23 0 FILE PASCAL

TOTAL FOR ALL FILES
L24 2 ((POLYGLUTAMINE REPEAT) OR (CAG REPEAT) OR POLYGLN) AND (TFA OR (TRIFLUOROACETIC ACID))

=> dup rem
ENTER L# LIST OR (END):l24
DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L24
L25 2 DUP REM L24 (0 DUPLICATES REMOVED)

=> d l25 ibib abs total

L25 ANSWER 1 OF 2 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2003:36505430 BIOTECHNO
TITLE: Role of histidine interruption in mitigating the pathological effects of long polyglutamine stretches in SCA1: A molecular approach
AUTHOR: Sen S.; Dash D.; Pasha S.; Brahmachari S.K.
CORPORATE SOURCE: S.K. Brahmachari, Inst. of Genom./Integrative Biology, CSIR, Mall Road, Delhi-110007, India.
E-mail: skb@cbt.res.in
SOURCE: Protein Science, (01 MAY 2003), 12/5 (953-962), 35 reference(s)
CODEN: PRCIEI ISSN: 0961-8368
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English

SUMMARY LANGUAGE: English
AN 2003:36505430 BIOTECHNO
AB Polyglutamine expansions, leading to aggregation, have been implicated in various neurodegenerative disorders. The range of repeats observed in normal individuals in most of these diseases is 19-36, whereas mutant proteins carry 40-81 repeats. In one such disorder, spinocerebellar ataxia (SCA1), it has been reported that certain individuals with expanded **polyglutamine repeats** in the disease range (Q.sub.1.sub.2HQHQ.sub.1.sub.2HQHQ.sub.1.sub.4.sub./.sub.1.sub.5) but with histidine interruptions were found to be phenotypically normal. To establish the role of histidine, a comparative study of conformational properties of model peptide sequences with (Q.sub.1.sub.2HQHQ.sub.1.sub.2 HQHQ.sub.1.sub.2) and without (Q.sub.4.sub.2) interruptions is presented here. Q.sub.1.sub.2HQHQ.sub.1.sub.2HQHQ.sub.1.sub.2 displays greater solubility and lesser aggregation propensity compared to uninterrupted Q.sub.4.sub.2 as well as much shorter Q.sub.2.sub.2. The solvent and temperature-driven conformational transitions (β structure .rfwdarw. random coil → α helix) displayed by these model polyQ stretches is also discussed in the present report. The study strengthens our earlier hypothesis of the importance of histidine interruptions in mitigating the pathogenicity of expanded polyglutamine tract at the SCA1 locus. The relatively lower propensity for aggregation observed in case of histidine interrupted stretches even in the disease range suggests that at a very low concentration, the protein aggregation in normal cells, is possibly not initiated at all or the disease onset is significantly delayed. Our present study also reveals that besides histidine interruption, proline interruption in polyglutamine stretches can lower their aggregation propensity.

L25 ANSWER 2 OF 2 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2001:32240515 BIOTECHNO
TITLE: Solubilization and disaggregation of polyglutamine peptides
AUTHOR: Chen S.; Wetzel R.
CORPORATE SOURCE: Dr. R. Wetzel, Graduate School of Medicine, R221 Univ. of Tennessee Med. Center, 1924 Alcoa Highway, Knoxville, TN 37920, United States.
E-mail: rwetzel@mc.utmck.edu
SOURCE: Protein Science, (2001), 10/4 (887-891), 16 reference(s)
CODEN: PRCIEI ISSN: 0961-8368
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2001:32240515 BIOTECHNO
AB A method is described for dissolving and disaggregating chemically synthesized polyglutamine peptides. Polyglutamine peptides longer than about Q.sub.2.sub.0 have been reported to be insoluble in water, but dissolution in - and evaporation from - a mixture of **trifluoroacetic acid** and hexafluoroisopropanol converts polyglutamine peptides up to at least Q.sub.4.sub.4 to a form readily soluble in aqueous buffers. This procedure also has a dramatic effect on peptides which appear to be completely soluble in water, by removing traces of aggregate that seed aggregation. The protocol makes possible solution studies - including in vitro aggregation experiments - on polyglutamine peptides with repeat lengths associated with increased risk of Huntington's Disease and other expanded **CAG repeat** diseases. It may also be useful in conducting reproducible, quantitative aggregation studies on other polypeptides.

=> ((polyglutamine repeat) or (CAG repeat) or polyGln) and (hexafluoroisopropanol or HFIP)

L26 0 FILE AGRICOLA
L27 1 FILE BIOTECHNO
L28 0 FILE CONFSCI
L29 0 FILE HEALSAFE
L30 0 FILE IMSDRUGCONF
L31 0 FILE LIFESCI
L32 0 FILE MEDICONF
L33 0 FILE PASCAL

TOTAL FOR ALL FILES
L34 1 ((POLYGLUTAMINE REPEAT) OR (CAG REPEAT) OR POLYGLN) AND (HEXAFLU OROISOPROPANOL OR HFIP)

=> d l34 ibib abs total

L34 ANSWER 1 OF 1 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2001:32240515 BIOTECHNO
TITLE: Solubilization and disaggregation of polyglutamine peptides
AUTHOR: Chen S.; Wetzel R.
CORPORATE SOURCE: Dr. R. Wetzel, Graduate School of Medicine, R221 Univ. of Tennessee Med. Center, 1924 Alcoa Highway, Knoxville, TN 37920, United States.
E-mail: rwetzel@mc.utmck.edu
SOURCE: Protein Science, (2001), 10/4 (887-891), 16 reference(s)
CODEN: PRCIEI ISSN: 0961-8368
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2001:32240515 BIOTECHNO
AB A method is described for dissolving and disaggregating chemically synthesized polyglutamine peptides. Polyglutamine peptides longer than about Q.sub.2.sub.0 have been reported to be insoluble in water, but dissolution in - and evaporation from - a mixture of trifluoroacetic acid and **hexafluoroisopropanol** converts polyglutamine peptides up to at least Q.sub.4.sub.4 to a form readily soluble in aqueous buffers. This procedure also has a dramatic effect on peptides which appear to be completely soluble in water, by removing traces of aggregate that seed aggregation. The protocol makes possible solution studies - including in vitro aggregation experiments - on polyglutamine peptides with repeat lengths associated with increased risk of Huntington's Disease and other expanded **CAG repeat** diseases. It may also be useful in conducting reproducible, quantitative aggregation studies on other polypeptides.

```
=> (polyglutamine or poly(gln) or (CAG repeat)) and (filament or aggregrate) and
diameter
MISSING OPERATOR 'POLY(GLN'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> (polyglutamine or (CAG repeat)) and (filament or aggregrate) and diameter
L1            0 FILE AGRICOLA
L2            0 FILE BIOTECHNO
L3            0 FILE CONFSCI
L4            0 FILE HEALSAFE
L5            0 FILE IMSDRUGCONF
L6            0 FILE LIFESCI
L7            0 FILE MEDICONF
L8            0 FILE PASCAL

TOTAL FOR ALL FILES
L9            0 (POLYGLUTAMINE OR (CAG REPEAT)) AND (FILAMENT OR AGGREGRATE)
                AND DIAMETER

=> (polyglutamine or (CAG repeat)) and (filament or aggregrate)
L10           1 FILE AGRICOLA
L11           7 FILE BIOTECHNO
L12           0 FILE CONFSCI
L13           0 FILE HEALSAFE
L14           0 FILE IMSDRUGCONF
L15           3 FILE LIFESCI
L16           0 FILE MEDICONF
L17           7 FILE PASCAL

TOTAL FOR ALL FILES
L18          18 (POLYGLUTAMINE OR (CAG REPEAT)) AND (FILAMENT OR AGGREGRATE)

=> dup rem
ENTER L# LIST OR (END):l18
DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L18
L19           13 DUP REM L18 (5 DUPLICATES REMOVED)

=> l19 and py<2004
L20           1 S L19
L21           1 FILE AGRICOLA
L22           7 S L19
L23           7 FILE BIOTECHNO
L24           0 S L19
'2004' NOT A VALID FIELD CODE
L25           0 FILE CONFSCI
L26           0 S L19
L27           0 FILE HEALSAFE
L28           0 S L19
L29           0 FILE IMSDRUGCONF
L30           2 S L19
L31           2 FILE LIFESCI
L32           0 S L19
'2004' NOT A VALID FIELD CODE
L33           0 FILE MEDICONF
L34           3 S L19
L35           3 FILE PASCAL

TOTAL FOR ALL FILES
L36          13 L19 AND PY<2004
```

=> d 136 ibib abs total

L36 ANSWER 1 OF 13 AGRICOLA Compiled and distributed by the National Agricultural Library of the Department of Agriculture of the United States of America. It contains copyrighted materials. All rights reserved. (2005) on STN

ACCESSION NUMBER: 2003:26217 AGRICOLA
DOCUMENT NUMBER: IND23322105
TITLE: A Drosophila homolog of the **polyglutamine** disease gene SCA2 is a dosage-sensitive regulator of actin **filament** formation.
AUTHOR(S): Satterfield, T.F.; Jackson, S.M.; Pallanck, L.J.
AVAILABILITY: DNAL (442.8 G28)
SOURCE: Genetics, **Dec 2002.** Vol. 162, No. 4. p. 1687-1702
Publisher: Bethesda, Md. : Genetics Society of America.
CODEN: GENTAE; ISSN: 0016-6731
NOTE: Includes references
PUB. COUNTRY: Maryland; United States
DOCUMENT TYPE: Article
FILE SEGMENT: U.S. Imprints not USDA, Experiment or Extension
LANGUAGE: English

L36 ANSWER 2 OF 13 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2003:36416961 BIOTECHNO
TITLE: Aggresomes protect cells by enhancing the degradation of toxic **polyglutamine**-containing protein
AUTHOR: Taylor J.P.; Tanaka F.; Robitschek J.; Sandoval C.M.; Taye A.; Markovic-Plese S.; Fischbeck K.H.
CORPORATE SOURCE: J.P. Taylor, Neurogenetics Branch, Natl. Inst. Neurol. Disorders/Stroke, National Institutes of Health, 10 Center Drive, Bethesda, MD 20892-1250, United States. E-mail: taylorjp@ninds.nih.gov
SOURCE: Human Molecular Genetics, **(01 APR 2003)**, 12/7 (749-757), 28 reference(s)
CODEN: HMGEE5 ISSN: 0964-6906
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:36416961 BIOTECHNO
AB Expression of misfolded protein in cultured cells frequently leads to the formation of juxtanuclear inclusions that have been termed 'aggresomes'. Aggresome formation is an active cellular response that involves trafficking of the offending protein along microtubules, reorganization of intermediate **filaments** and recruitment of components of the ubiquitin proteasome system. Whether aggresomes are benevolent or noxious is unknown, but they are of particular interest because of the appearance of similar inclusions in protein deposition diseases. Here we present evidence that aggresomes serve a cytoprotective function and are associated with accelerated turnover of mutant proteins. We show that mutant androgen receptor (AR), the protein responsible for X-linked spinobulbar muscular atrophy, forms insoluble aggregates and is toxic to cultured cells. Mutant AR was also found to form aggresomes in a process distinct from aggregation. Molecular and pharmacological interventions were used to disrupt aggresome formation, revealing their cytoprotective function. Aggresome-forming proteins were found to have an accelerated rate of turnover, and this turnover was slowed by inhibition of aggresome formation. Finally, we show that aggresome-forming proteins become membrane-bound and associate with lysosomal structures. Together, these findings suggest that aggresomes are cytoprotective, serving as cytoplasmic recruitment centers to facilitate degradation of toxic

proteins.

L36 ANSWER 3 OF 13 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2001:34280215 BIOTECHNO
TITLE: Identities of sequestered proteins in aggregates from cells with induced **polyglutamine** expression
AUTHOR: Suhr S.T.; Senut M.-C.; Whitelegge J.P.; Faull K.F.; Cuizon D.B.; Gage F.H.
CORPORATE SOURCE: F.H. Gage, Salk Inst. for Biological Studies, 10010 North Torrey Pines Rd., San Diego, CA 92037, United States.
E-mail: gage@salk.edu
SOURCE: Journal of Cell Biology, **(16 APR 2001)**, 153/2 (283-294), 52 reference(s)
CODEN: JCLBA3 ISSN: 0021-9525
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2001:34280215 BIOTECHNO
AB Proteins with expanded **polyglutamine** (polyQ) tracts have been linked to neurodegenerative diseases. One common characteristic of expanded-polyQ expression is the formation of intracellular aggregates (IAs). IAs purified from polyQ-expressing cells were dissociated and studied by protein blot assay and mass spectrometry to determine the identity, condition, and relative level of several proteins sequestered within aggregates. Most of the sequestered proteins comigrated with bands from control extracts, indicating that the sequestered proteins were intact and not irreversibly bound to the polyQ polymer. Among the proteins found sequestered at relatively high levels in purified IAs were ubiquitin, the cell cycle-regulating proteins p53 and mdm-2, HSP70, the global transcriptional regulator Tata-binding protein/TFIID, cytoskeleton proteins actin and 68-kD neurofilament, and proteins of the nuclear pore complex. These data reveal that IAs are highly complex structures with a multiplicity of contributing proteins.

L36 ANSWER 4 OF 13 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2000:30825603 BIOTECHNO
TITLE: Molecular characterization of human tensin
AUTHOR: Chen H.; Ishii A.; Wong W.-K.; Chen L.B.; Lo S.H.
CORPORATE SOURCE: S.H. Lo, Ctr. for Tissue Regeneration/Repair, Department of Orthopaedic Surgery, University of California-Davis, 4635 Second Avenue, Sacramento, CA 95817, United States.
E-mail: shlo@ucdavis.edu
SOURCE: Biochemical Journal, **(15 OCT 2000)**, 351/2 (403-411), 46 reference(s)
CODEN: BIJOAK ISSN: 0264-6021
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2000:30825603 BIOTECHNO
AB Tensin is a focal-adhesion molecule that binds to actin **filaments** and interacts with phosphotyrosine-containing proteins. To analyse tensin's function in mammals, we have cloned tensin cDNAs from human and cow. The isolated approx. 7.7-kb human cDNA contains an open reading frame encoding 1735 amino acid residues. The amino acid sequence of human tensin shares 60% identity with chicken tensin, and contains all the structural features described previously in chicken tensin. This includes the actin-binding domains, the Src homology domain 2, and the region similar to a tumour suppressor, PTEN. Two major differences between human and chicken tensin are (i) the lack of the first 54 residues present in

chicken tensin, and (ii) the addition of 34- and 38-residue inserts in human and bovine tensin. In addition, our interspecies sequencing data have uncovered the presence of a glutamine/**CAG repeat** that appears to have expanded in the course of evolution. Northern-blot analysis reveals a 10-kb message in most of the human tissues examined. An additional 9-kb message is detected in heart and skeletal muscles. The molecular mass predicted from the human cDNA is 185 kDa, although both endogenous and recombinant human tensin migrate as 220-kDa proteins on SDS/PAGE. The discrepancy is due to the unusually low electrophoretic mobility of the central region of the tensin polypeptide (residues 306-981). A survey of human prostate and breast cancer cell lines by Western-blot analysis shows a lack of tensin expression in most cancer cell lines, whereas these lines express considerable amounts of focal-adhesion molecules such as talin and focal-adhesion kinase. Finally, tensin is rapidly cleaved by a focal-adhesion protease, calpain II. Incubation of cells with a calpain inhibitor, MDL, prevented tensin cleavage and induced morphological change in these cells, suggesting that cleavage of tensin and other focal-adhesion constituents by calpain disrupts maintenance of normal cell shape.

L36 ANSWER 5 OF 13 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1999:30038076 BIOTECHNO
TITLE: **Polyglutamine** domain proteins with expanded repeats bind neurofilament, altering the neurofilament network
AUTHOR: Nagai Y.; Onodera O.; Strittmatter W.J.; Burke J.R.
CORPORATE SOURCE: J.R. Burke, Department of Medicine, Duke University Medical Center, Durham, NC 27710, United States.
E-mail: james.burke@duke.edu
SOURCE: Annals of the New York Academy of Sciences, (**1999**) 893/- (192-202), 49 reference(s)
CODEN: ANYAA0 ISSN: 0077-8923
DOCUMENT TYPE: Journal; Conference Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1999:30038076 BIOTECHNO
AB Proteins with expanded **polyglutamine** (polyQ) repeats cause eight inherited neurodegenerative diseases. Nuclear and cytoplasmic polyQ protein is a common feature of these diseases, but its role in cell death remains debatable. Since the neuronal intermediate **filament** network is composed of neurofilament (NF) and NF abnormalities occur in neurodegenerative diseases, we examined whether pathologic length polyQ domain proteins interact with NF. We expressed polyQ-green fluorescent fusion proteins (GFP) in a neuroblast cell line, TR1. Pathologic-length polyQ-GFP fusion proteins form large cytoplasmic aggregates surrounded by neurofilament. Immunoisolation of pathologic length polyQ proteins co-isolated 68 kD NF protein demonstrating molecular interaction. These observations suggest that polyQ interaction with NF is important in the pathogenesis of the **polyglutamine** repeat diseases.

L36 ANSWER 6 OF 13 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1999:29124713 BIOTECHNO
TITLE: Expanded **polyglutamine** domain proteins bind neurofilament and alter the neurofilament network
AUTHOR: Nagai Y.; Onodera O.; Chun J.; Strittmatter W.J.; Burke J.R.
CORPORATE SOURCE: J.R. Burke, Department of Medicine (Neurology), Deane Laboratory, Duke University Medical Center, Durham, NC 27710, United States.
E-mail: james.burke@duke.edu
SOURCE: Experimental Neurology, (**1999**), 155/2 (195-203), 50 reference(s)

CODEN: EXNEAC ISSN: 0014-4886
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1999:29124713 BIOTECHNO
AB Eight inherited neurodegenerative diseases are caused by genes with expanded **CAG repeats** coding for **polyglutamine** domains in the disease- producing proteins. The mechanism by which this expanded **polyglutamine** domain causes neurodegenerative disease is unknown, but nuclear and cytoplasmic **polyglutamine** protein aggregation is a common feature. In transfected COS7 cells, expanded **polyglutamine** proteins aggregate and disrupt the vimentin intermediate **filament** network. Since neurons have an intermediate **filament** network composed of neurofilament (NF) and NF abnormalities occur in neurodegenerative diseases, we examined whether pathologic-length **polyglutamine** domain proteins also interact with NF. We expressed varying lengths **polyglutamine** -green fluorescent protein fusion proteins in a neuroblast cell line, TR1. Pathologic-length **polyglutamine**-GFP fusion proteins formed large cytoplasmic aggregates surrounded by neurofilament. Immunoisolation of pathologic-length **polyglutamine** proteins coisolated 68- kDa NF protein demonstrating molecular interaction. These observations suggest that **polyglutamine** interaction with NF is important in the pathogenesis of the **polyglutamine** repeat diseases.

L36 ANSWER 7 OF 13 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1997:27464435 BIOTECHNO
TITLE: Oligomerization of expanded-**polyglutamine** domain fluorescent fusion proteins in cultured mammalian cells
AUTHOR: Onodera O.; Burke J.R.; Miller S.E.; Hester S.; Tsuji S.; Roses A.D.; Strittmatter W.J.
CORPORATE SOURCE: W.J. Strittmatter, Department of Medicine (Neurology), Duke University Medical Center, Durham, NC 27710, United States.
E-mail: warren@neuro.duke.edu
SOURCE: Biochemical and Biophysical Research Communications, (**1997**), 238/2 (599-605), 29 reference(s)
CODEN: BBRCA0 ISSN: 0006-291X
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1997:27464435 BIOTECHNO
AB Six inherited neurologic diseases, including Huntington's disease, result from the expansion of a CAG domain of the disease genes to produce a domain of more than 40 glutamines in the expressed protein. The mechanism by which expansion of this **polyglutamine** domain causes disease is unknown. Recent studies demonstrated oligomerization of **polyglutamine**-domain proteins in mammalian neurons. To study oligomerization of **polyglutamine** proteins and to identify heterologous protein interactions, varying length **polyglutamine** -green fluorescent protein fusion proteins were expressed in cultured COS-7 cells. The 19-and 35-glutamine fusion proteins (non-pathologic length) distributed diffusely throughout the cytoplasm. In contrast, 56- and 80-glutamine fusion proteins (pathologic length) formed fibrillar arrays resembling those previously observed in neurons in Huntington's disease and in a transgenic mouse model. These aggregates were intranuclear and intracytoplasmic. Intracytoplasmic aggregates were surrounded by collapsed intermediate **filaments**. The intermediate **filament** protein vimentin co-immunoisolated with expanded **polyglutamine** fusion proteins. This cellular model

will expedite investigations into oligomerization of **polyglutamine** proteins and their interactions with other proteins.

L36 ANSWER 8 OF 13 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1997:27116471 BIOTECHNO
TITLE: HIP-I: A huntingtin interacting protein isolated by the yeast two-hybrid system
AUTHOR: Wanker E.E.; Rovira C.; Scherzinger E.; Hasenbank R.; Walter S.; Tait D.; Colicelli J.; Lehrach H.
CORPORATE SOURCE: E.E. Wanker, Max Planck Inst. Molekulare Genetik, Ihnestrasse 73, 14195 Berlin (Dahlem), Germany.
SOURCE: Human Molecular Genetics, (**1997**), 6/3 (487-495), 42 reference(s)
CODEN: HMGEE5 ISSN: 0964-6906
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1997:27116471 BIOTECHNO
AB We report the discovery of the huntingtin interacting protein I (HIP-I) which binds specifically to the N-terminus of human huntingtin, both in the two-hybrid screen and in in vitro binding experiments. For the interaction in vivo, a protein region downstream of the **polyglutamine** stretch in huntingtin is essential. The HIP1 cDNA isolated by the two-hybrid screen encodes a 55 kDa fragment of a novel protein. Using an affinity-purified polyclonal antibody raised against recombinant HIP-I, a protein of 116 kDa was detected in brain extracts by Western blot analysis. The predicted amino acid sequence of the HIP-I fragment exhibits significant similarity to cytoskeleton proteins, suggesting that HIP-I and huntingtin play a functional role in the cell **filament** networks. The HIP1 gene is ubiquitously expressed in different brain regions at low level. HIP-I is enriched in human brain but can also be detected in other human tissues as well as in mouse brain. HIP-I and huntingtin behave almost identically during subcellular fractionation and both proteins are enriched in the membrane containing fractions.

L36 ANSWER 9 OF 13 LIFESCI COPYRIGHT 2005 CSA on STN
ACCESSION NUMBER: 2003:78741 LIFESCI
TITLE: The neuropathogenic contributions of lysosomal dysfunction
AUTHOR: Bahr, B.A.; Bendiske, J.
CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Connecticut, Storrs, CT 06269-2092, USA; E-mail: Bahr@uconn.edu
SOURCE: Journal of Neurochemistry [J. Neurochem.], (**20021100**) vol. 83, no. 3, pp. 481-489.
ISSN: 0022-3042.
DOCUMENT TYPE: Journal
TREATMENT CODE: General Review
FILE SEGMENT: N3
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Multiple lines of evidence implicate lysosomes in a variety of pathogenic events that produce neurodegeneration. Genetic mutations that cause specific enzyme deficiencies account for more than 40 lysosomal storage disorders. These mostly pre-adult diseases are associated with abnormal brain development and mental retardation. Such disorders are characterized by intracellular deposition and protein aggregation, events also found in age-related neurodegenerative diseases including (i) Alzheimer's disease and related tauopathies (ii) Lewy body disorders and synucleinopathies such as Parkinson's disease, and (iii) Huntington's disease and other **polyglutamine** expansion disorders. Of particular interest for this

review is evidence that alterations to the lysosomal system contribute to protein deposits associated with different types of age-related neurodegeneration. Lysosomes are in fact highly susceptible to free radical oxidative stress in the aging brain, leading to the gradual loss of their processing capacity over the lifespan of an individual. Several studies point to this lysosomal disturbance as being involved in amyloidogenic processing, formation of paired helical **filaments**, and the aggregation of alpha -synuclein and mutant huntingtin proteins. Most notably, experimentally induced lysosomal dysfunction, both in vitro and in vivo, recapitulates important pathological features of age-related diseases including the link between protein deposition and synaptic loss.

L36 ANSWER 10 OF 13 LIFESCI COPYRIGHT 2005 CSA on STN
ACCESSION NUMBER: 2003:45445 LIFESCI
TITLE: Amyloid-like Features of **Polyglutamine** Aggregates and Their Assembly Kinetics
AUTHOR: Chen, Songming; Berthelier, V.; Hamilton, J.B.; O'Nuallain, B.; Wetzel, R.
CORPORATE SOURCE: Graduate School of Medicine, University of Tennessee Medical Center, 1924 Alcoa Highway, Knoxville, TN 37920, USA
SOURCE: Biochemistry (Washington) [Biochemistry (Wash.)], (**20020611**) vol. 41, no. 23, pp. 7391-7399. ISSN: 0006-2960.
DOCUMENT TYPE: Journal
FILE SEGMENT: N3
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The repeat length-dependent tendency of the **polyglutamine** sequences of certain proteins to form aggregates may underlie the cytotoxicity of these sequences in expanded **CAG repeat** diseases such as Huntington's disease. We report here a number of features of various **polyglutamine** (polyGln) aggregates and their assembly pathways that bear a resemblance to generally recognized defining features of amyloid fibrils. PolyGln aggregation kinetics displays concentration and length dependence and a lag phase that can be abbreviated by seeding. PolyGln aggregates exhibit classical beta -sheet-rich circular dichroism spectra consistent with an amyloid-like substructure. The fundamental structural unit of all the in vitro aggregates described here is a **filament** about 3 nm in width, resembling the protofibrillar intermediates in amyloid fibril assembly. We observed these filamentous structures either as isolated threads, as components of ribbonlike sheets, or, rarely, in amyloid-like twisted fibrils. All of the polyGln aggregates described here bind thioflavin T and shift its fluorescence spectrum. Although all polyGln aggregates tested bind the dye Congo red, only aggregates of a relatively long polyGln peptide exhibit Congo red birefringence, and this birefringence is only observed in a small portion of these aggregates. Remarkably, a monoclonal antibody with high selectivity for a generic amyloid fibril conformational epitope is capable of binding polyGln aggregates. Thus, polyGln aggregates exhibit most of the characteristic features of amyloid, but the twisted fibril structure with Congo red birefringence is not the predominant form in the polyGln repeat length range studied here. We also find that polyGln peptides exhibit an unusual freezing-dependent aggregation that appears to be caused by the freeze concentration of peptide and/or buffer components. This is of both fundamental and practical significance. PolyGln aggregation is revealed to be a highly specific process consistent with a significant degree of order in the molecular structure of the product. This ordered structure, or the assembly process leading to it, may be responsible for the cell-specific neuronal degeneration observed in Huntington's and other expanded **CAG repeat** diseases.

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on STN
ACCESSION NUMBER: 2000-0295083 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2000 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Ubiquitinated filamentous inclusions in cerebellar dentate nucleus neurons in dentatorubral-pallidoluysian atrophy contain expanded **polyglutamine** stretches
AUTHOR: YAMADA M.; PIAO Y.-S.; TOYOSHIMA Y.; TSUJI S.; TAKAHASHI H.
CORPORATE SOURCE: Department of Pathology, Brain Research Institute, Niigata University, 1 Asahimachi, Niigata 951-8585, Japan; Department of Neurology, Brain Research Institute, Niigata University, 1 Asahimachi, Niigata 951-8585, Japan
SOURCE: Acta neuropathologica, **(2000)**, 99(6), 615-618, 22 refs.
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AB We have recently reported that, in addition to the widespread occurrence of ubiquitinated neuronal intranuclear inclusions (NIIs), the restricted occurrence of ubiquitinated intracytoplasmic filamentous inclusions in the neurons of the cerebellar dentate nucleus (CDN) is a characteristic feature of dentatorubral-pallidoluysian atrophy (DRPLA). Interestingly, these neuronal intracytoplasmic filamentous inclusions (NIFIs) were morphologically indistinguishable from the skein-like inclusions (SLIs) described previously in the spinal anterior horn cells in amyotrophic lateral sclerosis (ALS). In the present study, we examined immunohistochemically the CDN in ten patients with clinicopathologically and genetically confirmed DRPLA and the spinal anterior horns in five patients with sporadic ALS, using a monoclonal antibody (1C2) directed against long **polyglutamine** stretches. In all of the patients with DRPLA, both the NIFIs and the Nils were visualized clearly with 1C2. Conversely, in the patients with ALS all structures, including the SLIs, were completely negative. These findings indicate that in DRPLA, the NIFIs in the CDN are an alteration that is directly related to the causative gene abnormality (an expanded **CAG repeat** encoding **polyglutamine**) and that, from the molecular point of view, they are distinct from the SLIs in ALS.

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on STN
ACCESSION NUMBER: 1998-0270026 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 1998 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Huntingtin protein colocalizes with lesions of neurodegenerative diseases : An investigation in Huntington's, alzheimer's, and pick's diseases
AUTHOR: SINGHRAO S. K.; THOMAS P.; WOOD J. D.; MACMILLAN J. C.; NEAL J. W.; HARPER P. S.; JONES A. L.
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SOURCE: Experimental neurology, **(1998)**, 150(2), 213-222, 52 refs.
ISSN: 0014-4886 CODEN: EXNEAC

DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-9181, 354000075540180050

AN 1998-0270026 PASCAL

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AB Huntington's disease (HD) is an autosomal dominant neurodegenerative disease associated with a CAG trinucleotide repeat expansion in a large gene on chromosome 4. The gene encodes the protein huntingtin with a **polyglutamine** tract encoded by the **CAG repeat** at the N-terminus. The number of **CAG repeats** in HD are significantly increased (36 to 120+) compared with the normal population (8-39). The pathological mechanism associated with the expanded **CAG repeat** in HD is not clear but there is evidence that **polyglutamine** is directly neurotoxic. We have immunolocalized huntingtin with an in-house, well-characterised, polyclonal antibody in HD, Alzheimer's disease (AD), and Picks disease (PiD) brains. Control brain tissue sections were from head injured and cerebral ischaemia cases. In HD, huntingtin was immunopositive in the surviving but damaged neurons and reactive astrocytes of the caudate and putamen. However, in AD and PiD the immunostaining was largely restricted to the characteristic intracellular inclusion bodies associated with the disease process in each case. In AD, huntingtin was localized only in the intracellular neurofibrillary tangles and dystrophic neurites within the neuritic amyloid plaques but not with the amyloid. In PiD, strongly positive huntingtin immunostaining was present within cytoplasmic Pick bodies. Our findings suggest huntingtin selectively accumulates in association with abnormal intracytoplasmic and cytoskeletal **filaments** of neurons and glia in neurodegenerative diseases such as HD, AD, and PiD. Cells in the CNS appear sensitive to damage by the aggregated, toxic levels of huntingtin and evidence of its interaction with neurofilaments could provide information about its potential role in the aetiology of HD.

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TITLE (IN ENGLISH): Hereditary dentatorubral-pallidoluysian atrophy : ubiquitinated filamentous inclusions in the cerebellar dentate nucleus neurons

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AB We examined the cerebellar dentate nucleus (CDN) in 16 patients with hereditary dentatorubral-pallidoluysian atrophy (DRPLA), one of the neurodegenerative diseases caused by expansion of a **CAG repeat** encoding a **polyglutamine** tract in the disease protein. In all patients, some CDN neurons were found to contain ubiquitinated filamentous inclusions in their cytoplasm. On hematoxylin and eosin preparations, these filamentous inclusions were eosinophilic, basophilic or amphophilic, and were often found in areas of pale cytoplasm. Electron microscopy revealed that they consisted of bundles of **filaments** that were somewhat thicker than neurofilaments. These features of the present inclusions were indistinguishable from those of skein-like inclusions (SLI) previously described in the lower motor neurons in sporadic amyotrophic lateral sclerosis. We conclude that SLI can also occur in the CDN in DRPLA and believe that they reflect a characteristic pathological process in this disease.